Listing of Claims

The following listing of claims will replace all prior versions:

1. (Original) A method of improving immune function in a subject, comprising inhibiting a SPATIAL activity in a subject and thereby improving immune function in the subject, wherein immune function in the subject has been compromised by other than age-related immunodeficiency.

2. (Original) The method of claim 1, wherein immune function in the subject has been acutely compromised.

3. (Original) The method of claim 1, wherein the acute compromise of the immune system results from administration of a toxin to the subject, infection of the subject with an infectious agent, or treatment of the subject with radiation therapy.

4. (Original) The method of claim 3, wherein the toxin comprises at least one chemotherapeutic agent.

5. (Original) The method of claim 3, wherein the infectious agent comprises a virus.

6. (Original) The method of claim 6, wherein the virus is human immunodeficiency virus (HIV).

7. (Original) The method of claim 2, further comprising providing the subject with a bone marrow transplant.

8. (Original) The method of claim 1, wherein immune function in the subject has been compromised as a result of a disease.

9. (Original) The method of claim 8, wherein the disease is selected from the group consisting of HIV infection, acquired immunodeficiency syndrome (AIDS), autoimmune disease, thymic hypoplasia, chronic mucocutaneous candidiasis, severe combined immunodeficiency

(SCID), cellular immunodeficiency with immunoglobulins (Nezlof syndrome), immunodeficiency with thrombocytopenia and eczema (Wiskott-Aldrich syndrome), ataxia-telangiectasia, immunodeficiency with short-limbed dwarfism, immunodeficiency with thymoma, transcobalamin II deficiency, episodic lymphopenia with lymphotoxin, and idiopathic CD4 lymphocytopenia.

10. (Original) The method of claim 1, wherein inhibiting SPATIAL activity results in increasing thymocyte number in the subject.

11. (Original) The method of claim 10, wherein increasing thymocyte number comprises increasing DN thymocyte number.

12. (Original) The method of claim 1, wherein inhibiting a SPATIAL activity comprises inhibiting SPATIAL gene expression.

13. (Original) The method of claim 12, wherein SPATIAL gene expression is substantially eliminated.

14. (Original) The method of claim 1, wherein inhibiting SPATIAL activity comprises inhibiting a SPATIAL polypeptide activity.

15. (Original) The method of claim 1 further comprising administering to the subject a therapeutically effective amount of an agent that inhibits a SPATIAL activity.

16. (Original) The method of claim 15, wherein the agent comprises a small inhibitory RNA, an anti-sense nucleic acid, a ribozyme, an aptamer, a mirror-image aptamer, an Uba3 peptide, a SPATIAL peptide, an Uba3-specific antibody, or a SPATIAL-specific antibody.

17. (Original) The method of claim 15, wherein the agent inhibits an interaction between SPATIAL and Uba3.

18. (Original) The method of claim 17, wherein the agent comprises an Uba3 peptide, a SPATIAL peptide, an Uba3-specific antibody, a SPATIAL-specific antibody, an aptamer or a mirror-image aptamer.

19. (Original) The method of claim 17, wherein the agent comprises at least 15 consecutive amino acids of SEQ ID NO: 6.

20. (Original) The method of claim 19, wherein the agent consists of at least 15 consecutive amino acids between residues 183-308 of SEQ ID NO: 6.

21. (Original) A method of increasing thymocyte number in a subject having disease-associated T cell deficiency, comprising administering to a subject having a thymus and disease-associated T cell deficiency a therapeutically effective amount of an agent that inhibits a SPATIAL activity, thereby increasing thymocyte number in the subject.

22. (Original) The method of claim 21, wherein inhibiting a SPATIAL activity comprises inhibiting SPATIAL gene expression.

23. (Original) The method of claim 22, wherein the agent comprises a small inhibitory RNA (siRNA), an anti-sense nucleic acid, or a ribozyme.

24. (Original) The method of claim 22, wherein SPATIAL gene expression is substantially eliminated.

25. (Original) The method of claim 21, wherein the increasing thymocyte number comprises increasing DN thymocyte number in the thymus.

26. (Original) The method of claim 21, wherein the T cell deficiency comprises cellular immunodeficiency or combined immunodeficiency.

27. (Original) The method of claim 26, wherein the disease-associated T cell deficiency is selected from the group consisting of HIV infection, acquired immunodeficiency

syndrome (AIDS), autoimmune disease, thymic hypoplasia, chronic mucocutaneous candidiasis, severe combined immunodeficiency (SCID), cellular immunodeficiency with immunoglobulins (Nezlof syndrome), immunodeficiency with thrombocytopenia and eczema (Wiskott-Aldrich syndrome), ataxia-telangiectasia, immunodeficiency with short-limbed dwarfism, immunodeficiency with thymoma, transcobalamin II deficiency, episodic lymphopenia with lymphotoxin, and idiopathic CD4 lymphocytopenia.

28. (Original) The method of claim 26, wherein the subject has received a bone marrow transplant, chemotherapy or radiation therapy.

29. (Original) The method of claim 28, wherein the subject has received a bone marrow transplant.

30. (Original) The method of claim 29, wherein mature donor T cells are measurable in the blood of the subject prior to the time mature donor T cells are measurable in the blood of a second bone marrow transplant subject who did not receive an agent that inhibits SPATIAL activity.

31. (Original) The method of claim 29, wherein the agent is administered prior to the bone marrow transplant, concurrent with the bone marrow transplant, or after the bone marrow transplant.

32. (Original) The method of claim 31, wherein the agent is administered a sufficient period of time prior to bone marrow transplant to condition the thymus.

33. (Original) The method of claim 32, wherein the agent is administered up to about 30 days before the bone marrow transplant.

34. (Original) The method of claim 27, wherein the subject has HIV infection or acquired immunodeficiency syndrome (AIDS).

35. (Original) The method of claim 21, wherein the agent comprises a small inhibitory RNA, an anti-sense nucleic acid, a ribozyme, an aptamer, a mirror-image aptamer, an Uba3 peptide, a SPATIAL peptide, an Uba3-specific antibody, or a SPATIAL-specific antibody.

36. (Original) The method of claim 21, wherein inhibiting SPATIAL activity comprises inhibiting a SPATIAL polypeptide activity.

37. (Original) The method of claim 36, wherein the agent inhibits an interaction between SPATIAL and Uba3.

38. (Original) A method of increasing thymocyte number in a subject having a thymus, comprising administering to the subject a therapeutically effective amount of an agent that interferes with an interaction between SPATIAL and Uba3, thereby increasing thymocyte number in the subject.

39. (Original) The method of claim 38, wherein increasing thymocyte number comprises increasing DN thymocyte number in the thymus.

40. (Original) The method of claim 38, wherein the agent inhibits an interaction between SPATIAL and Uba3.

41. (Original) The method of claim 38, wherein the agent comprises an Uba3 peptide, a SPATIAL peptide, an Uba3-specific antibody, a SPATIAL-specific antibody, an aptamer or a mirror-image aptamer.

42. (Original) The method of claim 38, wherein the agent comprises at least 15 consecutive amino acids of SEQ ID NO: 6.

43. (Original) The method of claim 42, wherein the agent consists of at least 15 consecutive amino acids between residues 183-308 of SEQ ID NO: 6.

44. (Original) The method of claim 38, wherein the subject is immunodeficient.

45. (Original) The method of claim 44, wherein the immunodeficiency is cellular immunodeficiency or combined immunodeficiency.

46. (Original) The method of claim 45, wherein the immunodeficiency is an age-related immunodeficiency.

47. (Original) The method of claim 44, wherein the subject has received a bone marrow transplant, chemotherapy or radiation therapy.

48. (Original) The method of claim 44, wherein the subject has a disorder selected from the group consisting of HIV infection, acquired immunodeficiency syndrome (AIDS), autoimmune disease, thymic hypoplasia, chronic mucocutaneous candidiasis, severe combined immunodeficiency (SCID), cellular immunodeficiency with immunoglobulins (Nezlof syndrome), immunodeficiency with thrombocytopenia and eczema (Wiskott-Aldrich syndrome), ataxia-telangiectasia, immunodeficiency with short-limbed dwarfism, immunodeficiency with thymoma, transcobalamin II deficiency, episodic lymphopenia with lymphotoxin, and idiopathic CD4 lymphocytopenia.

49. (Original) A method for identifying an agent with potential for increasing thymocyte numbers, comprising determining SPATIAL inhibitory activity of the agent, wherein inhibition of SPATIAL activity by the agent identifies that the agent has potential for increasing thymocyte number.

50. (Currently Amended) The method of claim [[51]]49, further comprising determining whether administration of the agent to a Rag2 null mouse having a thymus results in the presence of naive T cells in the blood of the mouse after the mouse receives a bone marrow transplant.

51. (Original) A method of identifying an agent with potential for increasing thymocyte numbers, comprising:

providing a first component comprising an Uba3 polypeptide, a fragment thereof, or a functional variant thereof;

providing a second component comprising a SPATIAL polypeptide, a fragment thereof, or a functional variant thereof;

contacting the first component and the second component with an agent under conditions that would permit the first and second components to interact in the absence of the agent; and

determining whether the agent interferes with the interaction between the first and second components,

wherein interfering with the interaction between the first and second components indicates that the agent has potential for increasing thymocyte number.

52. (Original) The method of claim 51, wherein the first component comprises at least 15 consecutive amino acids of SEQ ID NO: 6 or at least 15 consecutive amino acids of a polypeptide having 80% sequence identity with SEQ ID NO: 6.

53. (Original) The method of claim 52, wherein the first component comprises at least 15 consecutive amino acids between residues 183-308 of SEQ ID NO: 6.

54. (Original) The method of claim 51, wherein the second component comprises at least 15 consecutive amino acids of SEQ ID NOs: 2 or 4 or at least 15 consecutive amino acids of a polypeptide having 80% sequence identity with SEQ ID NOs: 1 or 3.

55. (Original) A method of influencing cell growth, comprising modifying a SPATIAL activity in at least one cell, wherein modifying SPATIAL activity influences cell growth.

56. (Original) The method of claim 55, wherein modifying a SPATIAL activity comprises increasing SPATIAL activity.

57. (Original) The method of claim 56, wherein cell growth is inhibited.

58. (Original) The method of claim 57, wherein the cell(s) comprises neoplastic cell(s).

59. (Original) The method of claim 55, wherein modifying a SPATIAL activity comprises inhibiting SPATIAL activity.

60. (Original) The method of claim 55, wherein cell growth is enhanced.

61. (Original) The method of claim 60, wherein enhanced cell growth in the cell(s) results in increased thymocyte numbers.

62. (Original) A method of inhibiting cell growth, comprising introducing into at least one cell a polypeptide selected from the group consisting of:

(1) an amino acid sequence which has at least 80% sequence identity with SEQ ID NOs: 2 or 4 and has an activity of SPATIAL;

(2) a conservative variant of SEQ ID NOs: 2 or 4 that has an activity of SPATIAL;

(3) a fragment of at least fifteen consecutive amino acid residues of SEQ ID NOs: 2 or 4 that has an activity of SPATIAL;

(4) at least residues 21-197, at least residues 91-197, or at least residues 145-197 of SEQ ID NO: 2;

(5) at least residues 21-231, at least residues 91-176, or at least residues 91-231 of SEQ ID NO: 4; and

(6) SEQ ID NOs: 2 or 4;

wherein introducing the polypeptide into the cell(s) inhibits cell growth.

63. (Original) The method of claim 62, wherein the cell(s) comprise neoplastic cell(s).

64. (Original) A method of inhibiting cell growth, comprising expressing in at least one cell a nucleic acid sequence selected from the group consisting of:

(1) a nucleic acid sequence having at least 80% sequence identity with SEQ ID NOs: 1 or 3, which encodes a polypeptide having an activity of SPATIAL;

(2) a nucleic acid sequence comprising at least fifteen consecutive residues of SEQ ID NOs: 1 or 3, which encodes a polypeptide having an activity of SPATIAL;

(3) a nucleic acid sequence comprising at least residues 144-674, at least residues 354-674, or at least residues 516-674 of SEQ ID NO: 1;

(4) a nucleic acid sequence comprising at least residues 144-776, at least residues 354-611, or at least residues 354-776 of SEQ ID NO: 3; and

(5) a nucleic acid sequence comprising SEQ ID NOs: 1 or 3;

wherein expressing the nucleic acid sequence in the cell(s) inhibits cell growth.

65. (Original) The method of claim 64, wherein the cell(s) comprise neoplastic cell(s).

66. (Original) A method of treating neoplasia in a subject, comprising administering to a subject a therapeutically effective amount of a cell cycle inhibitory agent comprising:

(1) an amino acid sequence which is at least 80% homologous to SEQ ID NOs: 2 or 4 and has an activity of SPATIAL;

(2) a conservative variant of SEQ ID NOs: 2 or 4 that has an activity of SPATIAL;

(3) a fragment of at least fifteen consecutive amino acid residues of SEQ ID NOs: 2 or 4 that has an activity of SPATIAL;

(4) at least residues 21-197, at least residues 91-197 or at least residues 145-197 of SEQ ID NO: 2;

(5) at least residues 21-231, at least residues 91-176, or at least residues 91-231 of SEQ ID NO: 4; or

(6) SEQ ID NOs: 2 or 4.